

JAN 2 9 2008

1 Used in Lieu of PTO/SB/08A/B (Based on PTO 01-08 version)

Substitute for form 1449/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 1 of 10

	Complete if Known					
Application Number	10/632,428-Conf. #4377					
Filing Date	August 1, 2003					
First Named Inventor	David Bebbington					
Art Unit	1624					
Examiner Name	D. R. Rao					
Attorney Docket Number	030682.0001-US01					

			U.S. PA	TENT DOCUMENTS	
Examiner Initials*	Cite No.1	Document Number Number-Kind Code ² (<i>if known</i>)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	AA	US-3,133,081	05/12/1964	Lafferty et al.	
****	AB	US-3,755,322	08/28/1973	Winter et al.	
	AC	US-3,935,183	01/27/1976	Baron et al.	
	AD	US-3,998,951	12/21/1976	Harnish et al.	
	AE	US-4,051,252	09/27/1977	Mayer et al.	-
	AF	US-4,493,726	01/15/1985	Burdeska et al.	
	AG	US-4,540,698	09/10/1985	Ishikawa et al.	
	AH	US-4,711,951	12/08/1987	Axen et al.	
	AI	US-5,124,441	06/23/1992	Carlsson et al.	
-	AJ	US-5,710,158	01/20/1998	Myers et al.	
	AK	US-5,916,908	06/29/1999	Giese et al.	
	AL	US-5,972,946	10/26/1999	Murata et al.	
	AM	US-6,093,716	07/25/2000	Davis et al.	
-	AN	US-6,184,226	02/06/2001	Chakravarty et al.	
	AO	US-6,200,977	03/13/2001	Cushing et al.	
	AP	US-6,277,989	08/21/2001	Chakravarty et al.	
	AQ		12/17/2002	Hale et al.	
	AR	US-6,495,582	03/04/2003	Hale et al.	
		US-6,528,509	03/04/2003		
	AS	US-6,528,513		Cushing et al. Mandeville, III et al.	
	AT	US-6,558,657	05/06/2003		
	AU	US-6,562,971	05/13/2003	Frauenkron et al.	
	AV	US-6,569,499	05/27/2003	Grammatica et al.	
	AW	US-6,579,983	06/17/2003	Batchelor et al.	
	AX	US-6,589,958	07/08/2003	Frietze	
	AY	US-6,593,326	07/15/2003	Bradbury et al.	
	AZ	US-6,610,677	08/26/2003	Davies et al.	
	AA1	US-6,613,776	09/02/2003	Knegtel et al.	
	AB1	US-6,638,926	10/28/2003	Davies et al.	
	AC1	US-6,641,579	11/04/2003	Bernardi et al.	
	AD1	US-6,642,227	11/04/2003	Cao et al.	
	AE1	US-6,653,300	11/25/2003	Bebbington et al.	
	AF1	US-6,653,301	11/25/2003_	Bebbington et al.	
	AG1	US-6,656,939	12/02/2003	Bebbington et al.	
	AH1	US-6,660,731	12/09/2003	Bebbington et al.	
	AI1	US-6,664,247	12/16/2003	Bebbington et al.	
	AJ1	US-6,689,778	02/10/2004	Bemis et al.	
	AK1	US-6,696,452	02/24/2004	Davies et al.	
	AL1	US-6,716,851		Cai et al.	
	AM1	US-6,727,251	04/27/2004	Bebbington et al.	
	AN1	US-6,743,791	06/01/2004	Cao et al.	
	AO1	US-6,825,190	11/30/2004	Moon et al.	
	AP1	US-6,838,464	01/04/2005	Pease et al.	
	AQ1	US-6,841,579 B1	01/11/2005	Plowman et al.	
	AR1	US-6,846,928		Bebbington et al.	
	AS1	US-6,884,804	04/26/2005	Choon-Moon	

Sub	stitute for form 1449/PTO			Complete if Known		
""				Application Number	10/632,428-Conf. #4377	
l IN	IFORMATION	I DI	SCLOSURE	Filing Date	August 1, 2003	
l s	TATEMENT B	3Y /	APPLICANT	First Named Inventor	David Bebbington	
				Art Unit	1624	
	(Use as many sheets as necessary)			Examiner Name	D. R. Rao	
Sheet	2	of	10	Attorney Docket Number	030682.0001-US01	

r - 1			
AT1	US-6,919,338	07/19/2005	Mortlock et al.
AU1	US-6,949,544	09/27/2005	Bethiel et al.
AV1	US-6,989,385	01/24/2006	Bebbington et al.
AW1		03/07/2006	Bebbington et al.
AX1	US-7,084,159	08/01/2006	Cao et al.
AY1	US-7,087,603	08/08/2006	Bebbington et al.
AZ1	US-7,091,343	08/15/2006	Bebbington et al.
AA2	US-7,098,330	08/29/2006	Bebbington et al.
AB2	US-7,115,739	10/03/2006	Bebbington et al.
AC2	US-7,179,826	02/20/2007	Bebbington et al.
AD2	US-7,253,187	08/07/2007	Cao et al.
AE2	US-7,304,061	12/04/2007	Hale et al.
AF2	US-2002/0052386	02/16/2001	Armistead et al.
AG2	US-2002/0065270	12/22/2000	Moriarty et al.
AH2	US-2003/0064982	09/14/2001	Davies et al.
Al2	US-2003/0069248	10/02/2001	Chakravarty et al.
AJ2	US-2003/0096813	04/19/2002	Cao et al.
AK2	US-2003/0105090	12/19/2001	Bebbington et al.
AL2	US-2003/0199526	12/09/2002	Choquette et al.
AM2	US-2003/0207873	04/10/2002	Harrington et al.
AN2	US-2004/0009981	03/14/2003	Bebbington et al.
AO2	US-2004/0097531	07/09/2003	Ledeboer et al.
AP2	US-2004/0157893	11/25/2003	Bebbington et al.
AQ2	US-2004/0167141	02/10/2004	Bebbington et al.
AR2	US-2004/0214814	12/19/2001	Bebbington et al.
AS2	US-2005/0038023	08/01/2003	Bebbington et al.
AT2	US-2005/0234059	03/10/2005	Hale et al.
AU2	US-2006/0270660	08/09/2006	Charrier et al.

	FOREIGN PATENT DOCUMENTS								
Examiner Initials*	Cite No.1	Foreign Patent Document Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)	Publication Date _MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T⁵			
L	BA	EP 0,019,811 A1	12/10/1980	Ciba-Geigy AG		1			
{	BB	EP 0,136,976	04/10/1985	Ciba-Geigy AG					
}	ВС	EP 0,302,312 A2	02/08/1989	Bayer AG	į.				
1	BD	GB 2 052 487 A	01/28/1981	Ciba-Geigy AG	j				
1	BE	JP 06-065237	03/08/1994	Nissan Chem. Ind., Ltd.	ì				
1	BF	JP 10-130150	05/19/1998	Dainippon Pharmaceutical Co., Ltd.					
i P	BG	JP 2000-026421	01/25/2000=	Kumiai Chem Ind. Co. Ltd.	7				
	вн	WO 00/12497	03/09/2000	Scios Inc.		= >			
i	ВІ	WO 00/21955	04/20/2000	AstraZeneca AB	7	الا			
7	BJ	WO 00/38675	07/06/2000_	Smith Klein Beecham, PLC	÷,				
1	ВК	WO 00/39101	07/06/2000	AstraZeneca AB	ż				
1	BL	WO 00/42029	07/20/2000	Warner-Lambert Company					

Sub	stitute for form 1449/PT	·o		Complete if Known		
				Application Number	10/632,428-Conf. #4377	
l IN	IFORMATIO	ON DIS	CLOSURE	Filing Date	August 1, 2003	
S	TATEMENT	BY A	PPLICANT	First Named Inventor	David Bebbington	
				Art Unit	1624	
	(Use as many sheets as necessary)			Examiner Name	D. R. Rao	
Sheet	3	of	10	Attorney Docket Number	030682.0001-US01	

1	ВМ	WO 00/59509	10/12/2000	Novartis AG	16.	
	BN	WO 00/78757	12/28/2000	Shionogi Bioresearch Corp.		
· ·	во	WO 01/12621	02/22/2001	Vertex Pharmaceuticals Incorporated	J	
	BP	WO 01/25220	04/12/2001	Kinetix Pharmaceuticals Inc.		
a inde	BQ	WO 01/39777	06/07/2001	OSI Pharmaceuticals, Inc.		
1	BR	WO 01/40215	06/07/2001	Pfizer Products Inc.		
7	BS	WO 01/44242	06/21/2001	Bristol-Myers Squibb Co.		
121	ВТ	WO 01/47879	07/05/2001	Icos Corporation		
, , , , , , , , , , , , , , , , , , ,	BU	WO 01/47897	07/05/2001	Pharmacopeia, Inc. and Bristol-Myers Squibb Company		
	BV	WO 01/60816	08/23/2001	Amgen Inc.		
<i>"</i> .	BW	WO 01/64655	09/07/2001	AstraZeneca AB	7	
	вх	WO 01/74768	10/11/2001	Vertex Pharmaceuticals Incorporated		
1 1	BY	WO 01/79198	10/25/2001	Agouron Pharmaceuticals, Inc.		
	BZ	WO 02/057259	07/25/2002	Vertex Pharmaceuticals Incorporated		
Į.	BA1	WO 02/059111	08/01/2002	Vertex Pharmaceuticals Incorporated		
	BB1	WO 02/059112	08/01/2002	Vertex Pharmaceuticals Incorporated		
	BC1	WO 02/062789	08/15/2002	Vertex Pharmaceuticals Incorporated		
	BD1	WO 02/066461	08/29/2002	Vertex Pharmaceuticals Incorporated		
	BE1	WO 02/068415	09/06/2002	Vertex Pharmaceuticals Incorporated		
	BF1	WO 02/08244	01/31/2002	Schering Corp.		
	BG1	WO 02/18346	03/07/2002	Pfizer Products Inc.		
	BH1	WO 02/22601	03/21/2002	Vertex Pharmaceuticals Incorporated		
	BI1	WO 02/22602	03/21/2002	Vertex Pharmaceuticals Incorporated		
	BJ1	WO 02/22603	03/21/2002	Vertex Pharmaceuticals Incorporated		
	BK1	WO 02/22604	03/21/2002	Vertex Pharmaceuticals Incorporated		
	BL1	WO 02/22605	03/21/2002	Vertex Pharmaceuticals Incorporated		
	BM1	WO 02/22606	03/21/2002	Vertex Pharmaceuticals Incorporated		
	BN1	WO 02/22607	03/21/2002	Vertex Pharmaceuticals Incorporated		
	BO1	WO 02/22608	03/21/2002	Vertex Pharmaceuticals Incorporated		

Sub	estitute for form 1449/PTO			Complete if Known		
				Application Number	10/632,428-Conf. #4377	
IN	IFORMATION	N DI	SCLOSURE	Filing Date	August 1, 2003	
S	TATEMENT	BY A	APPLICANT	First Named Inventor	David Bebbington	
				Art Unit	1624	
	(Use as many sheets as necessary)			Examiner Name	D. R. Rao	
Sheet	4	of	10	Attorney Docket Number	030682.0001-US01	

	BP1	WO 02/24667	03/28/2002	Merck Patent GMBH		
	BQ1	WO 02/47690	06/20/2002	Cytovia, Inc.		
	BR1	WO 02/50065	06/27/2002	Vertex Pharmaceuticals		
				Incorporated		
	BS1	WO 02/50066	06/27/2002	Vertex Pharmaceuticals		
			ļ	Incorporated		
	BT1	WO 02/79197	10/10/2002	Vertex Pharmaceuticals		
<u> </u>		1110 0 1100000	10/04/0000	Incorporated		<u> </u>
	BU1	WO 04/00833	12/31/2003	Vertex Pharmaceuticals		
	BV1	WO 04/13140	02/12/2004	Incorporated Vertex Pharmaceuticals	-	
	PVI	VVO 04/13140	02/12/2004	Incorporated		
	BW1	WO 93/22681	11/11/1993	Neurogen Corporation		_
		WO 95/09851	04/13/1995	· 		
	BY1	WO 95/15758	06/15/1995	Rhone-Poulenc Rorer		
		1.00 00, 10.00	30, 10, 1000	Pharmaceuticals Inc.		
	BZ1	WO 96/14843	05/23/1996	Cor Therapeutics, Inc.		
	BA2	WO 97/09325	03/13/1997	Signal Pharmaceuticals, Inc.		
	BB2	WO 97/19065	05/29/1997	Celltech Therapeutics Limited		
	BC2	WO 98/02434	01/22/1998	Glaxo Group Limited		
	BD2	WO 98/11095	03/19/1998	Celltech Therapeutics Limited		
	BE2	WO 98/14450	04/09/1998	Novartis AG		
	BF2	WO 98/16502	04/23/1998	Warner-Lambert Company		
	BG2	WO 98/38171	09/03/1998	Signal Pharmaceuticals, Inc.		
	BH2	WO 99/18781	04/22/1999	Cytovia, Inc.		
	BI2	WO 99/41253	08/19/1999	Tularik Inc.		
	BJ2	WO 99/47154	09/23/1999	Cytovia, Inc.		
	BK2	WO 99/62518	12/09/1999	Cadus Pharmaceutical		
				Corporation		
	BL2	WO 99/65897	12/23/1999	Chiron Corporation		

Examiner		Date	
Signature		Considered	

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. \(^1\) Applicant's unique citation designation number (optional). \(^2\) See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. \(^3\) Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). \(^4\) For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. \(^5\) Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. \(^6\) Applicant is to place a check mark here if English language Translation is attached.

NON PATENT LITERATURE DOCUMENTS							
Examiner Initials	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²				
	CA	Agarwal, N. et al., "Suitably Functionalized Pyrimidines as Potential Antimycotic Agents", Bioorg. Med. Chem. Lett., 10, 8, 703-706 (2000).					
	СВ	Ali, N.M. et al, "Palladium-Catalyzed Cross Coupling Reactions of Arylboronic Acids with Pi- Deficient Heteroaryl Chlorides" Tetrahedron, 48 (37), 8117-8126 (1992).					

Subst	titute for form 1449/PTO			Complete if Known		
				Application Number	10/632,428-Conf. #4377	
IN	FORMATION	1 DI	SCLOSURE	Filing Date	August 1, 2003	
SI	TATEMENT E	3Y A	APPLICANT	First Named Inventor	David Bebbington	
				Art Unit	1624	
	(Use as many sheets as necessary)			Examiner Name	D. R. Rao	
Sheet	5	of	10	Attorney Docket Number	030682.0001-US01	

cc	Alonso, M. et al., "GSK-3 Inhibitors: Discoveries and Developments", Current Medicinal Chemistry, 11, 755-763 (2004).	
CD	Anderson, Neil G. "Requirement for integration of signals from two distinct phosphorylation pathways for activation of MAP kinase." Nature, 343, 651-653 (1990)	
CE	Anonymous, "Vertex Inhibitors of Aurora-2, glycogen synthase kinase-3 and Src Kinase", Expert Opin. Ther. Patents, 14(3): 439-443 (2004)	
CF	Baig, G.U. et al., "Triazines and Related Products. Part 28' Conversion of 3-Aryl-I-(2-cyanopheny1) triazenes into 3-Arylquinazolin-4(3H)-ones with Formamide" J. Chem. Soc. Perkin Trans. I, 2765-2766 (1984).	
CG	Baig, Ghouse Unissa et al. "Triazines and related products. Part 27. Thermolysis of 4-anilino-1,2,3-benzotriazines," <i>J. Chem., Soc., Perkin Trans.</i> 1(5): 999-1003 (1984)	
СН	Banker, G.S. et al., "Modern Pharmaceutics", 3rd ed., Marcel Dekker, New York 1996, pages 451 & 596.	
СІ	Biagi, G. et al., "Synthesis of 4,6-Disubstituted and 4,5,6-Trisubstituted-2-Phenyl-pyrimidines and their Affinity Towards A1 Adenosine Receptors", IL Farmaco., 52(1), 61-65 (1997).	
C1	Biscardi, J.S. et al., "c-Src, Receptor Tyrosine Kinases, and Human Cancer", Adv. Cancer Res., 76, 61 (1999).	
СК	Bischoff, J.R., et al., "A homologue of Drosophila aurora kinase is oncogenic and amplified in human colorectal cancers", The EMBO Journal, 17(11): 3052–3065 (1998).	
CL	Bischoff, J.R., et al., "The Aurora/IpI1p kinase family: regulators of chromosome segregation and cytokinesis", CELL BIOLOGY, 9, 454-459 (1999).	
СМ	Bjorbaek, C. et al, "Divergent Functional Roles for p90rsk Kinase Domains", J. Biol. Chem., 270(32), 18848-18552 (1995).	
CN	Bokemeyer, D. et al., "Multiple intracellular MAP kinase signaling cascades", Kidney Int., 49, 1187-1198 (1996).	
со	Bolen, J.B. et al., "Activation of pp60c-src protein kinase activity in human colon carcinoma", PNAS, 84, 2251-2255 (1987).	
СР	Boschelli et al., "Small molecule inhibitors of Src family kinases", Drugs of the Future, 25(7): 717-736 (2000).	
CQ	Brownlees, J. et al., "Tau phosphorylation in transgenic mice expressing glycogen synthase kinase-3beta transgenes", Neuroreport., 8(15), 3251-5 (1997).	
CR	Brunswick, D.J. et al., "Cyclic Amidines. Part XXII. Novel Isomerism of Disubstituted Tricycioquinazolines and Molecular Orientations in Carcinogenesis", J. Chem. SOC. (C), 2641-2647 (1970).	
cs	Campbell, S.F. et al., "2,4-Diamino-6,7-dimethoxyquinazolines. 3.2-(4-Heterocyclylpiperazin-l-yl) Derivatives as α1-Adrenoceptor Antagonists and Antihypertensive Agents," J. Med. Chem., 30, 1794-1798 (1987).	
СТ	CAPLUS listing Accession No. 1994:292136, Nakajima, Y. et al., "Pyrazoles agricultural and horticultural bactericides," JP 06065237 (1994).	
cu	Casanova, B. et al., "Revisión crítica de la patogenia actual de la esclerosis múltiple y futuras direcciones posibles," Rev. Neurol., 28 (9): 909-915 (1999).	
cv	Chalmers, D.T. et al., "Corticotrophin-releasing factor receptors: from molecular biology to drug design," TiPS, 17, 769-776 (2001).	
cw	Charpiot, B. et al., "Quinazolines: Combined type 3 and 4 phosphodiesterase inhibitors", Bioorg. Med. Chem. Lett., 8(20), 2891-2896 (1998).	
СХ	Chen, R.H. et al., "Phosphorylation of the c-Fos transrepression domain by mitogen-activated protein kinase and 90-kDa ribosomal S6 kinase", Proc. Natl. Acad. Sci. USA, 90, 10952-10956 (1993).	

Subs	stitute for form 1449/PT	го		Complete if Known		
				Application Number	10/632,428-Conf. #4377	
IN	FORMATIC	ON DIS	CLOSURE	Filing Date	August 1, 2003	
STATEMENT BY APPLICANT				First Named Inventor	David Bebbington	
				Art Unit	1624	
	(Use as many sheets as necessary)			Examiner Name	D. R. Rao	
Sheet	6	of	10	Attorney Docket Number 030682.0001-US01		

CY	Cline, G.W. et al., "Effects of a Novel Glycogen Synthase Kinase-3 Inhibitor on Insulin-Stimulated Glucose Metabolism in Zucker Diabetic Fatty (fa/fa) Rats," Diabetes, 51, 2903-2910 (2002).
CZ	Coghlan, M.P. et al., "Selective small molecule inhibitors of glycogen synthase kinase-3 modulate glycogen metabolism and gene transcription", Chemistry & Biology,7, 793-803 2000.
CA1	Cohen, P. et al., "The renaissance of GSK3," Nat. Rev. Mol. Cell Biol., 2, 769-776 (2001).
CB1	Cohen, P., "Dissection of the Protein Phosphorylation Cascades Involved in Insulin and Growth Factor Action", Biochem. Soc. Trans., 21, 555-567 (1993).
CC1	Coleman, R.A., "The Biological Evaluation of New Compounds" in Medicinal Chemistry: Principles and Practice, King, Frank D. ed, Royal Society of Chemistry, 53-66 (1994).
CD1	Crespo, M.I. et al., "Design, Synthesis, and Biological Activities of New Thieno[3,2-d]pyrimidines as Selective Type 4 Phosphodiesterase Inhibitors", J. Med. Chem., 41 (21), 4021-4035 (1998).
CE1	Crews, C.M. et al., "The Primary Structure of MEK, a Protein Kinase That Phosphorylates the ERK Gene Product", Science, 258, 478-480 (1992).
CF1	Cross, D.A.E. et al., "The inhibition of glycogen synthase kinase-3 by insulin or insulin-like growth factor 1 in the rat skeletal muscle cell line L6 is blocked by wortmannin, but not by rapamycin: evidence that wortmannin blocks activation of the mitogen-activated protein kinase pathway in L6 cells between Ras and Raf", Biochem J., 303: 21–26 (1994).
CG1	Curd, F.H.S. et al, "Synthetic antimalarials. Part XVII. Some aminoalkylaminoquinoline derivatives", J. Chem. Soc., 899 – 909 (1947).
CH1	D'Atri, G. et al., "Novel pyrimidine and 1,3,5-triazine hypolipemic agents", J. Med. Chem. 27(12), 1621 – 1629 (1984).
CI1	Damasio, A.R., "Alzheimer's Disease and Related Dementias," in Cecil Textbook of Medicine, 20th ed., 2: 1992-1996 (1996).
CJ1	Douglas, et al. "Introduction to Viral Disease" in Cecil Textbook of Medicine, 20th Ed., Vol. 2, 1739-1749 (1996).
CK1	Eldar-Finkelman, H. et al., "Challenges and opportunities with glycogen synthase kinase-3 inhibitors for insulin resistance and Type 2 diabetes treatment," Expert Opinion on Investigational Drugs, 12(9): 1511-1519 (2003).
CL1	Fedorynski, M. et al., "Synthesis of 1-Arycyclopropanecarbonitriles under Phase-transfer Catalytic Conditions", Org. Prep. Proced. Int., 27(3), 355-359 (1995).
CM1	Fischer, P.M. et al., "Inhibitors of Cyclin-Dependent Kinases as Anti-Cancer Therapeutics", Current Med. Chem., 7, 1213-1245 (2000).
CN1	Fisher A., "Therapeutic Strategies in Alzheimer's Disease: M1 Muscarinic Agonists," Jpn. J. Pharmacol., 84(2):101-12 (2000).
CO1	Fox T. et al., "A single amino acid substitution makes ERK2 susceptible to pyridinyl imidazole inhibitors of p38 MAP kinase", Protein Sci., 7: 2249-2255 (1998).
CP1	Frame, M.C., "Src in cancer: deregulation and consequences for cell behaviour," Biochimica et Biophysica Acta., 1602, 114–130 (2002).
CQ1	Frampton, J.E. et al., "Pentoxifylline (Oxpentifylline) - A Review of its Therapeutic Efficacy in the Management of Peripheral Vascular and Cerebrovascular Disorder," Drugs & Aging, 7(6): 480-503 (1995).
CR1	Frey, R.S. et al., "Involvement of Extracellular Signal-regulated Kinase 2 and Stress-activated Protein Kinase/Jun N-Terminal Kinase Activation by Transforming Growth Factor β in the Negative Growth Control of Breast Cancer Cells", Cancer Res., 57, 628-633 (1997).
CS1	Fry, D.W. et al., "Inhibitors of cyclin-dependent kinases as therapeutic agents for the treatment of cancer", Current Opin. Oncol. Endoc. & Metab. Investig., 2-40-59 (2000).

Substitute for form 1449/PTO				Complete if Known		
0000		. •		Application Number	10/632,428-Conf. #4377	
IN	FORMATION	ON DI	SCLOSURE	Filing Date	August 1, 2003	
SI	TATEMEN'	T BY	APPLICANT	First Named Inventor	David Bebbington	
		. –		Art Unit	1624	
	(Use as many	sheets as	necessary)	Examiner Name	D. R. Rao	
Sheet	7	of	10	Attorney Docket Number	030682.0001-US01	

CT1	Ganellin, C.R., "Past Approaches to Discovering New Drugs as Medicines" in Medicinal Chemistry, Principles and Practices. King, Frank D. ed, Royal Society of Chemistry, 189-205 (1994).
CU1	Garigipati, R.S., "An efficient conversion of nitriles to amidines", Tetrahedron Lett., 31(14), 1969-1972 (1990).
CV1	Gershon, H. et al., "Pyrimidines. 7. A Study of the Chlorination of Pyrimidines with Phosphorus Oxychloride in the Presence of N,N-Dimethylaniline", J. Heterocyclic Chem., 21, 1161-1167 (1984).
CW1	Glossary of Class Names of Organic Compounds and Reactive Intermediates Based on Structure found from http://www.chem.qmul.ac.uk/iupac/class/index.html (last visited on November 18, 2007).
CX1	Gnecco, D. et al., "An Improved Preparation of 1-Methyl-4-Cyano-4-phenylpiperidine", Org. Prep. Proced. Int., 18 (4), 478-480 (1996).
CY1	Hamdane, M. et al., "Pin 1 - A Therapeutic Target in Alzheimer Neurodegeneration," J. Mol. Neurosci., 19(3): 275-87 (2002).
CZ1	Haq, S. et al., "Glycogen Synthase Kinase-3β Is a Negative Regulator of Cardiomyocyte Hypertrophy", J. Cell Biol., 151(1), 117-129 (2000).
CA2	Hardt, S.E. et al., "Glycogen Synthase Kinase-3β - A Novel Regulator of Cardiac Hypertrophy and Development," Circulation Research, 90: 1055-1063 (2002).
CB2	Harrington, E.A. et al., "VX-680, a potent and selective small-molecule inhibitor of the Aurora kinases, suppresses tumor growth in vivo," Nat. Med., 10(3): 262-267 (2004).
CC2	Haworth, R.D. et al., "Synthetic antimalarials. Part XXVII. Some derivatives of phthalazine, quinoxaline, and isoquinoline", J. Chem. Soc., 777 – 782 (1948).
CD2	Heaney, F., et al., "Pyrimidine annelated heterocycles-synthesis and cycloaddition of the first pyrimido[1,4]diazepine N-oxides," <i>J. Chem. Soc., Perkin Trans.</i> , 1:622-632 (2001)
CE2	Henriksen, E.J. et al., "Modulation of muscle insulin resistance by selective inhibition of GSK-3 in Zucker diabetic fatty rats," Am. J. Physiol. Endocrinol. Metab., 284: E892–E900 (2003).
CF2	Heutink, P., "Untangling tau-related dementia", Hum. Mol. Genet., 9(6): 979-986 (2000).
CG2	Ife, R.J. et al., "Reversible Inhibitors of the Gastric (H+/K+)-ATPase. 5. Substituted 2,4-Diaminoquinazolines and Thienopyrimidines", J. Med. Chem., 38(14); 2763 – 2773 (1995).
CH2	IUPAC Compendium of Chemical Terminology on a definition of "aliphatic compounds" found from http://www.chemsoc.org/chembytes/goldbook/index.htm (last visited on November 18, 2007).
Cl2	Ivashchenko A. V. et al., "Synethsis and Study of Heteroaromatic Ligands Containing a Pyrimidine Ring", Khim. Geterotsikl. Soedin., (12), 1673-7, (1980).
CJ2	Jambhekar, S.S., "Biopharmaceutical Properties of Drug Substances" in Principles of Medicinal Chemistry, 4th ed., 12-24, (1995).
CK2	Jeffery, J.E. et al., "Synthesis of sibutramine, a novel cyclobutylalkylamine useful in the treatment of obesity, and its major human metabolites", J. Chem. Soc., Perkin Trans. 1, 21, 2583-2589 (1996).
CL2	Katzung, Bertram G., Basic and Clinical Pharmacology, 7th Edition, 1998, pp. 881-884.
CM2	Kelarev, V.I. et al., "Synthesis of amino derivatives of 1,3,5-triazine containing 1,3-4-thiadiazole fragments," IZVESTIYA VYSSHIKH UCHEBNKH ZAVEDENII, KHIMIYA I KHIMICHESKAYA TEKHNOLOGIYA, 40(5): 27-32 (1997).
CN2	Kim, L. et al., "GSK3, a master switch regulating cell-fate specification and tumorigenesis," Current Opinion in Genetics & Development, 10:508-514 (2000).
CO2	Kim, Y.Z. et al., "Synthesis and Antimicrobial Activity of Novel [(3-Aminopyrimidiniumyl)thio]methyl Cephalosporins", J. Med. Chem., 37(22); 3828 - 3833 (1994).

Sub	ostitute for form 1449/PTO			Complete if Known		
				Application Number	10/632,428-Conf. #4377	
11	NFORMATION	N DI	SCLOSURE	Filing Date	August 1, 2003	
S	TATEMENT I	3Y /	APPLICANT	First Named Inventor	David Bebbington	
				Art Unit	1624	
	(Use as many sh	eets as	s necessary)	Examiner Name	D. R. Rao	
Sheet	8	of	10	Attorney Docket Number 030682.0001-US01		

CP2	Kimura, M. et al., "Cell Cycle-dependent Expression and Centrosome Localization of a Third Human Aurora/lpl1-related Protein Kinase, AlK3", J. Biol. Chem., 274(11), 7334-7340 (1999).	
CQ2	Klein, P.S. et al., "A molecular mechanism for the effect of lithium on development", PNAS, 93: 8455-8459 (1996).	
CR2	Layzer, R.B., "Section Five - Degenerative Diseases of the Nervous System" in Cecil Textbook of Medicine, 20th ed., 2: 2050-2057 (1996).	
CS2	Lee, S.J. et al., "Discovery of Potent Cyclic GMP Phosphodiesterase Inhibitors. 2-Pyridyl- and 2-Imidazolylquinazolines Possessing Cyclic GMP Phosphodiesterase and Thromboxane Synthesis Inhibitory Activities," J. Med . Chem., 38 (18): 3547-3557 (1995).	
CT2	Lovestone, S. et al., "Alzheimer's disease-like phosphorylation of the microtubule-associated protein tau by glycogen synthase kinase-3 in transfected mammalian cells", Curr. Biol., 4(12), 1077-86 (1994).	
CU2	Lübbers, T. et al., "Design, synthesis, and structure–activity relationship studies of ATP analogues as DNA gyrase inhibitors", Bioorg. Med. Chem. Lett., 10, 8, 821-826 (2000).	
CV2	Lutz, M.L. et al., "Overexpression and Activation of the Tyrosine Kinase Src in Human Pancreatic Carcimona", Biochem. Biophys. Res. 243, 503-508 (1998).	
CW2	Lynch, S.A. et al., "Increased Expression of the src Proto-Oncogene in Hairy Cell Leukemia and a Subgroup of B-Cell Lymphomas", Leukemia, 7(9), 1416-1422 (1993).	
CX2	Lyrer, P., "Neue Ansätze in der Akutbehandlung des zerebrovaskulären Insultes." Schweiz. Med. Woohen Schr., 124(45); 2005-2012 (1994).	
CY2	Mani, S. et al., "Cyclin-dependent kinase: novel anticancer agents", Exp. Opin. Invest. Drugs., 8, 1849-1870 (2000).	
CZ2	Masaki, T. et al., "pp60c-src Activation in Hepatocellular Carcinoma of Humans and LEC Rats", Hapatology, 27, 1257 (1998).	
CA3	Massillon, D. et al., "Identification of the glycogenic compound 5-iodotubercidin as a general protein kinase inhibitor", Biochem J., 299: 123–128 (1994).	
CB3	Medwid, Jeffrey B. et al., "Preparation of triazolo'1, 5-cipyrimidines as potential antiasthma agents," <i>J. Med. Chem.</i> , 33(4): 1230 -1241 (1990)	
CC3	Molina, T.J. et al., "Profound block in thymocyte development in mice lacking p56lck", Nature, 357, 161-164 (1992).	
CD3	Moodie, S.A. et al., "Complexes of Ras-GTP with Raf-1 and Mitogen-Activated Protein Kinase Kinase", Science, 260(5114), 1658-1661 (1993).	
CE3	Moss, R.A. et al., "Conversion of 'Obstinate' Nitriles to Amidines by Garigipati's Reaction", Tetrahedron Lett., 36(48), 8761-8764 (1995).	
CF3	Myers, M.R. et al., "The synthesis and SAR of new 4-(N-alkyl-N-phenyl)amino-6,7-dimethoxyquinazolines and 4-(N-alkyl-N-phenyl)aminopyrazolo[3,4-d]pyrimidines, inhibitors of CSF-1R tyrosine kinase activity", Bioorg. Med. Chem. Lett., 7, 4, 421-424 (1997).	
CG3	Nair, M.D., et al., "3-Chloroisocarbostyril & Its Chlorination Products", Indian J. Chem., vol. 5, 467-470 (1967).	
СНЗ	Namikawa, Kazuhiko et al., "Akt/Protein Kinase B Prevents Injury-Induced Motoneuron Death and Accelerates Axonal Regeneration." The Journal of Neuroscience, 20(8), 2875-2886 (2000)	
CI3	Nezu, Y., et al., "Dimethoxypyrimidines as Novel Herbicides. part 1. Synthesis and Herbicidal Activity of Dimethoxyphanoxyphenoxypyrimidines and Analogues," <i>Pestic. Sci.</i> , 47(2): 103-113 (1996).	
CJ3	Nezu, Y., et al., "Dimethoxypyrimidines as Novel Herbicides. part 2. Synthesis and Herbicidal Activity of O-Pyrimidinylasalicylates and Analogues," <i>Pestic. Sci.</i> , 47(2): 115-124 (1996).	
СКЗ	Nigg, E.A., "Mitotic Kinases as Regulators of Cell Division and its Checkpoints," Nat. Rev. Mol. Cell Biol., 2: 21-32 (2001).	

Substitute for form 1449/PTO				Complete if Known		
		•		Application Number	10/632,428-Conf. #4377	
IN	NFORMATIO	N DISC	CLOSURE	Filing Date	August 1, 2003	
S	TATEMENT	BY AP	PLICANT	First Named Inventor	David Bebbington	
				Art Unit	1624	
	(Use as many sheets as necessary)			Examiner Name	D. R. Rao	
Sheet	9	of	10	Attorney Docket Number	030682.0001-US01	

CL3	Noell, C.W. et al., "Potential Purine Antagonists. XX. The Preparation and Reactions of Some Methylthiopurines", J. Am. Chem. Soc., 81(22), 5997 – 6007 (1959).
СМЗ	Nomenclature found from http://www.cem.msu.edu/~reusch/VirtualText/nomen1.htm (last visited on November 18, 2007).
CN3	Norman, M.H. et al., "Structure-Activity Relationships of a Series of Pyrrolo[3,2-d]pyrimidine Derivatives and Related Compounds as Neuropeptide Y5 Receptor Antagonists", J. Med. Chem., 43(22), 4288 -4312 (2000).
CO3	Nugent, R.A. et al., "Pyrimidine Thioethers: A Novel Class of HIV-1 Reverse Transcriptase Inhibitors with Activity Against BHAP-Resistant HIV", J. Med. Chem., 41, 3793-3803 (1998).
CP3	Okafor, Charles O., "Studies in the Heterocyclic Series. 1,3,9-Triazaphenothiazine Ring System, a New Phenothiazine Ring," <i>J. Org. Chem.</i> , 40(19):2753-2755 (1975).
CQ3	Parnell, E.W., "2-Cyano-4-nitrophenylhydrazine and 3-Amino-5-nitroindazole", J. Chem. Soc., 2363-2365 (1959).
CR3	Pei, J. et al., "Distribution, Levels, and Activity of Glycogen Synthase Kinase-3 in the Alzheimer Disease Brain", J. Neuropathol. Exp. Neurology, 56, 70-78 (1997)
CS3	Prasad, G. et al., "18-Crown-6 as a catalyst in the dialkylation of o-nitrophenacyl derivatives", J. Org. Chem., 25, 7188-7190 (1991).
СТЗ	Raingeaud, J. et al., "MMK3- and MMK6-Regulated Gene Expression Is Mediated by p38 Mitogen-Activated Protein Kinase Signal Transduction Pathway", Mol. Cell. Biol., 16, 1247-1255 (1996).
CU3	Rogers, E. et al., "The aurora kinase AIR-2 functions in the release of chromosome cohesion in Caenorhabditis elegans meiosis," J. Cell Biol., 157(2): 219–229 (2002).
CV3	Rosen, N. et al., "Analysis of pp60c-src Protein Kinase Activity in Human Tumor Cell Lines and Tissues", J.Biol. Chem., 261, 13754-13759 (1986).
CW3	Rouse, J. et al., "A Novel Kinase Cascade Triggered by Stress and Heat Shock That Stimulates MAPKAP Kinase-2 and Phosphorylation of the Small Heat Shock Proteins", Cell, 78, 1027-1037 (1994).
СХЗ	Rueeger, H et al., "Design, synthesis and SAR of a series of 2-substituted 4-amino-quinazoline neuropeptide Y Y5 receptor antagonists", Bioorg. Med. Chem. Lett., 10(11), 1175-1180 (2000).
CY3	Shikhaliev, K.S. et al., "Heterocyclization of quinazol-2-ylguanidines. 1. Reaction with amino acids", Chem. Heterocycl. Compd., 35 (7), 818-820 (1999).
CZ3	Simone, J.V., "Oncology: Introduction" in Cecil Textbook in Medicine, 20th ed., Vol. 1, 1004-1010 (1996).
CA4	Singh, S.P. et al., "Synthesis & Mass Spectra of Some Substituted 2-(2'-Benzazolylamino)pyrimidines", Indian J. Chem. Sect. B, 22(1); 37-42 (1983).
CB4	Singhal, N. et al., "Synthesis and Antimalarial Activity of Some New Quinazoline Derivatives", Indian Chem. Soc., 61, 690-693 (1984).
CC4	Sivaraman, V.S., et al., "Hyperexpression of Mitogen-activated Protein Kinase in Human Breast Cancer", J. Clin. Invest., 99(7), 1478-1483 (1997).
CD4	Soriano, P. et al., "Targeted Disruption of the C-SRC Proto-Oncogene Leads to Osteopetrosis in Mice," Cell, 64: 693-702, (1991).
CE4	Staley, C.A. et al., "Decreased Tumorigenicity of a Human Colon Adenocarcinoma Cell Line by an Antisense Expression Vector Specific for c-Src", Cell Growth Diff., 8, 269-274 (1997).
CF4	Suzuki, S. et al., "Application of electrogenerated triphenylmethyl anion as a base for alkylation of arylacetic esters and arylacetonitriles and isomerization of allylbenzenes", Can. J. Chem., 72(2): 357–361 (1994).

Sut	ostitute for form 1449/PTO			Complete if Known		
Out	outdie for form 1 1 for 1 c			Application Number	10/632,428-Conf. #4377	
11	NFORMATIO	N DI	SCLOSURE	Filing Date	August 1, 2003	
S	TATEMENT	BY /	APPLICANT	First Named Inventor	David Bebbington	
				Art Unit	1624	
	(Use as many si	heets as	s necessary)	Examiner Name	D. R. Rao	
Sheet	10	of	10	Attorney Docket Number	030682.0001-US01	

CG4	Takashima, K. et al., "Tau Protein Kinase I is Essential for Amyloid ß-Protein-Induced Neurotoxicity", PNAS 90, 7789-7793 (1993).	
CH4	Takayanagi, H. et al., "Suppression of arthritic bone destruction by adenovirus-mediated csk gene transfer to synoviocytes and osteoclasts", J. Clin. Invest., 104, 137-146 (1999).	
CI4	Talamonti, M.S. et al., "Increase in activity and level of pp60c-src in progressive stages of human colorectal cancer", J Clin Invest., 91(1): 53-60 (1993).	
CJ4	Tanaka, T.U. et al., "Evidence that the lpl1-Sli15 (Aurora Kinase-INCENP) Complex Promotes Chromosome Bi-orientation by Altering Kinetochore-Spindle Pole Connections," Cell, 108, 317-329 (2002).	
CK4	Tanji, K. et al., "Purines. X. Reactivities of Methyl Groups on 9-Phenylpurines: Condensation with an Aldehyde or an Ester, and Oxidation with Selenium Dioxide", Chem. Phar. Bull., 40 (1), 227-229 (1992).	
CL4	The CONDENSED CHEMICAL DICTIONARY, Sixth Edition by Arthur and Elizabeth Rose, 38 (1961).	
CM4	Ti, J. et al., "Anticandidal activity of pyrimidine-peptide conjugates", J. Med. Chem., 23(8), 913 – 918 (1980).	
CN4	Toriyabe, Keiji et al: "Preparation of sulfur-containing arylthiazoles and insecticides", Chemica Abstracts, 132(8):93314 (2000).	
CO4	Traxler P. et al., "Use of a pharmacophore model for the design of EGF-R Tyrosine Kinase Inhibitors: 4-(Phenylamino)Pyrazolo[3, 4-d]pyrimidines," <i>Journal of Medicinal Chemistry</i> , 40(22): 3601-3616 (1997)	
CP4	Venugopalan, B. et al., "Synthesis and antimalarial activity of pyrido[3,2-f)quinozalines and their N-oxides", Indian J. Chem. Sect. B, 34, 9, 778-790 (1995).	
CQ4	Wagman, A.S. et all, "Discovery and Development of GSK3 Inhibitors for the Treatment of Type 2 Diabetes," Current Pharmaceutical Design, 10, 1105-1137 (2004).	
CR4	Warner, S.L. et al, "Targeting Aurora-2 Kinase in Cancer," Mol. Cancer Thera., 2, 589-585, 2003.	
CS4	Whelchel, A. et al., "Inhibition of ERK Activation Attenuates Endothelin-stimulated Airway Smooth Muscle Cell Proliferation", Am. J. Respir. Cell Mol. Biol., 16, 589-596 (1997).	
CT4	Wiener, J.R., "Decreased Src Tyrosine Kinase Activity Inhibits Malignant Human Ovarian Cancer Tumor Growth in a Nude Mouse Model", Clin. Cancer Res., 5, 2164-2170 (1999).	
CU4	Wolft, Manfred E., "Burger's Medicinal Chemistry, 5th ed., Part 1" John Wiley & Sons, 1995, pages 975-977.	
CV4	Yuan, Z.Q. et al., "Frequent activation of AKT2 and induction of apoptosis by inhibition of phosphoinositide-3-OH kinase/Akt pathway in human ovarian cancer", Oncogene, 19, 2324-2330 (2000).	
CW4	Zhang, Z. et al., "Destabilization of ß-catenin by mutations in presenilin-1 potentiates neuronal apoptosis", Nature, 395, 698-702 (1998).	

Examiner	Date	
Signature	Considered	

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹Applicant's unique citation designation number (optional). ²Applicant is to place a check mark here if English language Translation is attached.